

Synthesis of Dimethyl Glutarate from Cyclobutanone and Dimethyl Carbonate over Solid Base Catalysts

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A facile route for the synthesis of dimethyl glutarate (DMG) from cyclobutanone and dimethyl carbonate (DMC) in the presence of solid base catalysts has been developed. It was found that the intermediate carbomethoxycyclobutanone (CMCB) was produced from cyclobutanone with DMC in the first step, and then CMCB was further converted to DMG by reacting with a methoxide group. The role of the basic catalysts can be mainly ascribed to the activation of cyclobutanone *via* the abstraction of a proton in the α -position by base sites, and solid bases with moderate strength, such as MgO, favor the formation of DMG.

Key Words : Dimethyl glutarate, Cyclobutanone, Dimethyl carbonate, Solid base catalysts

Introduction

Dimethyl glutarate (DMG) is a fine chemical that is widely used as an industrial solvent for pharmaceuticals, perfumes, plastics and other organic compounds.¹ It is usually obtained by esterification of glutaric acid with methanol.² However, this process has several limitations, such as harsh reaction conditions, lack of chemoselectivity, and significant corrosion and separation problems. In particular, a stoichiometric amount of water is produced in this esterification process, which required tedious procedures for disposal.³

Recently, much attention has been given to dimethyl carbonate (DMC), which is an important derivative of C1 chemistry, due to its versatile chemical properties and low toxicity. It is believed to be an ideal additive for gasoline, because of its high oxygen content (53%) and good blending properties with octane.⁴ As an environmentally benign building block, it is mainly used in methylation and carbonylation reactions as a safe substitute for methyl halides, dimethyl sulfate and phosgene.^{5,6} In the presence of a base, it can also react with a number of nucleophilic anions generated from different substrates such as ketones, amines, oximes, indoles, and phenols to give the corresponding methoxycarbonylation products.⁷⁻¹²

In the 1990s, Selva first reported a route for the synthesis of α,ω -dicarboxylic acid diesters by methoxycarbonylation of alicyclic ketones with organic carbonates using as K_2CO_3 catalyst.¹³ Later, others reported that DMC reacted with alicyclic ketones to produce dimethyl esters in the presence of homogenous catalysts such as CH_3OK , Cs_2CO_3 -crown ether and organic amines.¹⁴⁻¹⁶ However, to the best of our knowledge, the reaction of cyclobutanone with DMC has not been investigated previously, which might be an attractive synthetic route for the production of DMG due to the safe and clean chemical process. Moreover, homogenous reactions give rise to problems with separation of the products and catalyst reuse. Over the past decade, research

on the synthesis of fine chemicals using solid bases as catalysts has become an important topic.^{17,18} Particularly, a lot of works were devoted to the research of DMC utilization by using solid bases.¹⁹⁻²¹ The replacement of homogeneous bases by solid base catalysts in DMC utilization has the advantages of decreasing corrosion and environmental problems, while allowing easier separation and recovery of the products, catalyst and solvent. Especially, in our previous work, it was found that solid bases like metal oxides (such as MgO) could show excellent activity in DMC utilization when compared with homogenous catalysts (such as NaOH and CH_3ONa).^{22,23}

Thus, a novel and facile one-pot approach to the production of dimethyl glutarate is developed *via* the methoxycarbonylation of cyclobutanone with dimethyl carbonate over solid base catalysts (such as metallic oxides), and the function of the solid base catalysts is discussed in the present work.

Materials and Methods

Preparation of Catalysts. CaO, MgO and ZrO_2 were prepared by thermal decomposition of calcium carbonate ($CaCO_3$, Tianjin Kermel Chemical Reagent Co. Ltd, A.R. grade) at 800 °C for 2 h, magnesium hydroxide ($Mg(OH)_2$, Tianjin Kermel Chemical Reagent Co. Ltd, A.R. grade) at 500 °C for 5 h, and zirconium hydroxide ($Zr(OH)_4$, Tianjin Kermel Chemical Reagent Co. Ltd, A.R. grade) at 500 °C for 5 h, respectively, under a nitrogen atmosphere. Lanthana (La_2O_3 , Tianjin Kermel Chemical Reagent Co. Ltd, A.R. grade) and alumina (Al_2O_3 , Tianjin Kermel Chemical Reagent Co. Ltd, A.R. grade) were calcined at 700 °C and 500 °C respectively for 5 h in N_2 before use. A series of Al/MgO catalysts with molar ratios of 0.01-0.3 were also prepared using the impregnation method. The desired amount of aluminum isopropoxide was dissolved in ethanol before adding to $Mg(OH)_2$ to form the impregnated samples. The

samples were dried at 100 °C overnight and then thermally decomposed at 500 °C for 5 h to afford Al/MgO catalysts.

The specific surface area and pore volume of the samples were obtained by the BET method. The samples were degassed at 350 °C for 5 h under vacuum (10^{-6} Torr) prior to the measurements, and nitrogen adsorption/desorption isotherms were obtained at -196 °C on a Micromeritics ASAP-2000 instrument (Norcross, GA).

CO₂-Temperature programmed desorption (CO₂-TPD) measurements were performed using Ar as a carrier gas. Catalyst samples (0.10 g, 40-60 mesh) were pretreated in Ar at 500 °C for 2 h. After the samples were cooled down to room temperature, CO₂ was pulsed into the reactor until saturation was reached. Once physically adsorbed CO₂ was purged by the carrier gas, the CO₂-TPD experiments were carried out from 20 °C to 800 °C with a heating rate of 10 °C/min under Ar flow (50 mL/min), and the effluent was analyzed with a gas chromatograph that employed a thermal conductivity detector. The amount of basic sites was quantified through calculating the areas of desorption peaks in the CO₂-TPD profiles using K₂CO₃ as primary standard.

Experimental Setup and Procedure. The reaction was carried out in an autoclave reactor, which was composed of a 150 mL stainless-steel autoclave and a magnetic stirrer (revolving at a rate of 1000 rpm). Cyclobutanone (5.00 g), DMC (25.74 g) and the catalyst (0.45 g) were charged into the autoclave and then the resulting mixture was heated to 260 °C within 30 min. After running at 260 °C for 5 h under autogenous pressure (about 1-3 MPa in the temperature region from 200 °C to 280 °C), the reactor was cooled in situ to room temperature. The catalyst was removed by rapid filtration and the liquid products were analyzed by a gas chromatograph (GC-920, Shanghai Haixin Chromatograph Instrument Co. Ltd) with a flame ionization detector and a HP-5 column. The selectivity is defined as $m_A/\Sigma m_A \times 100\%$, where m_A is the weight of product A, and m_A is the total weight of the products.

Results and Discussion

Catalyst Characterization. Figure 1 depicts the TPD profiles of CO₂ desorbed from ZrO₂, MgO, La₂O₃ and CaO. CaO exhibited strong basic sites with a sharp desorption peak at 540 °C. La₂O₃ showed relatively strong base strength with a CO₂ desorption peak at 430 °C. For MgO, there were three desorption peaks at 100 °C, 190 °C and 300 °C, suggesting that MgO had both weak and moderate strength basic sites, but for ZrO₂ a single CO₂ desorption peak at 140 °C was observed, indicating that only weak basic sites were present. The base strength follows the order: CaO > La₂O₃ > MgO > ZrO₂, but the basic numbers of the catalysts (the amount of basic sites per unit area of catalysts) decreased in the order: CaO > MgO > La₂O₃ > ZrO₂ (see Table 1). After addition of alumina into MgO, three desorption peaks were also found, at around at 120 °C, 200 °C and 290 °C for the resulting Al/MgO samples, which suggested that the addition of alumina did not change the basic strength of

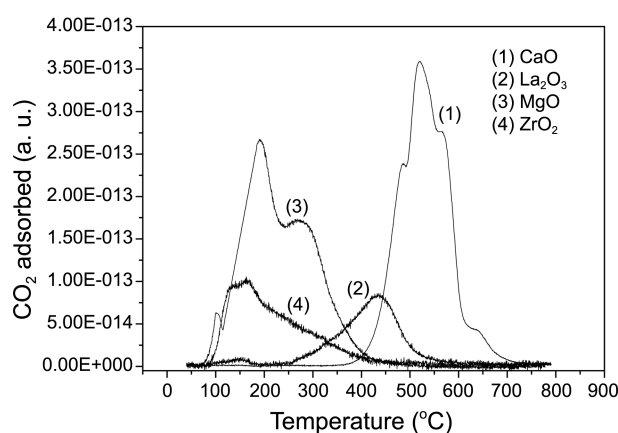


Figure 1. CO₂-TPD profiles of solid bases.

Table 1. CO₂ uptake of solid bases

Catalyst	BET surface area (m ² /g)	CO ₂ uptake	
		mmol/g	mmol/m ²
ZrO ₂	151.3	6.79E-03	4.49E-05
La ₂ O ₃	8.7	4.53E-04	5.21E-05
CaO	12.1	8.02E-02	6.63E-03
MgO	134.5	9.71E-03	7.22E-05
Al/MgO(0.01)	112.4	7.49E-03	6.66E-05
Al/MgO(0.05)	101.9	6.44E-03	6.32E-05
Al/MgO(0.1)	93.8	5.82E-03	6.20E-05
Al/MgO(0.2)	82.2	4.87E-03	5.92E-05
Al/MgO(0.3)	71.3	4.03E-03	5.65E-05

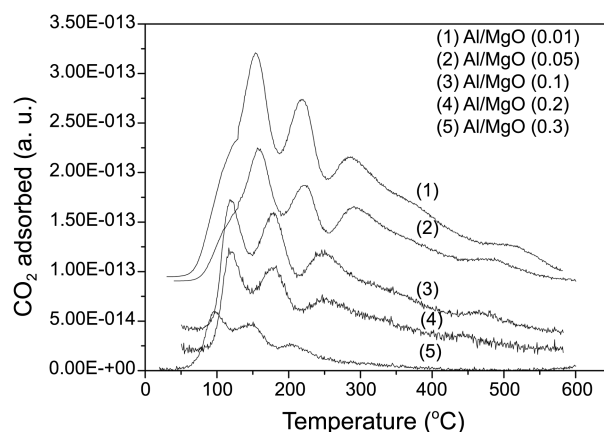


Figure 2. CO₂-TPD profiles of MgO with different Al contents.

MgO (see Figure 2), but the basic number decreased with increasing Al contents (see Table 1).

Catalytic Performance. The reaction was carried out within the temperature range from 200 °C to 280 °C and the main by-products were carbomethoxycyclobutanone (CMCB), which might be the intermediate methoxycarbonylation product from cyclobutanone with DMC. The self-condensation products of cyclobutanone (2-cyclobutylidencyclobutanone), methylation products (2-methyl-cyclobutanone and dimethyl 2-methylglutarate) and attendant methylation

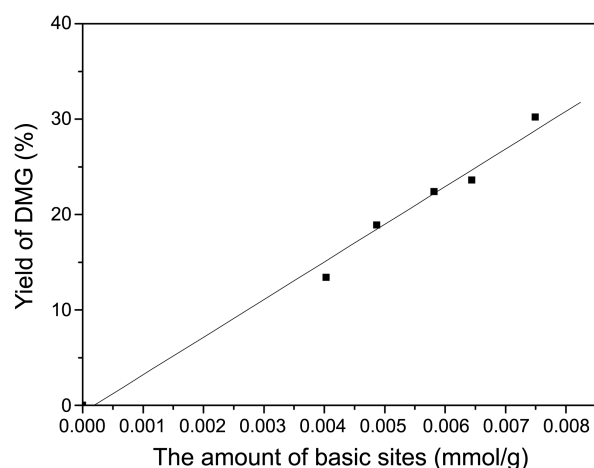
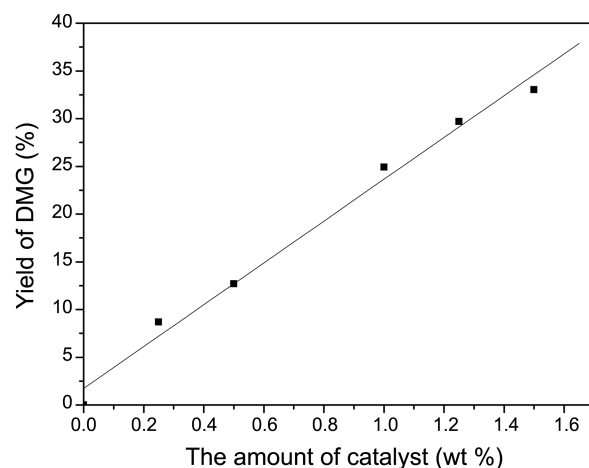
Table 2. Synthesis of DMG from DMC and cyclobutanone over solid bases

Entry ^a	Catalyst ^b	Time (h)	Cyclobutanone conversion (%)	Selectivity (%) ^c			
				DMG	CMCB	ACP	MP
1	-	-	-	-	-	-	-
2	H β	5	25.8	0.69	1.37	97.9	-
3	Al ₂ O ₃	5	37.9	0.28	0.84	98.9	-
4	K ₂ CO ₃	5	40.6	23.4	9.68	13.8	53.1 ^d
5	NaOH	5	53.7	33.6	20.1	32.4	13.9
6	CH ₃ ONa	5	61.9	41.5	20.3	28.7	9.50
7	ZrO ₂	1	13.5	12.8	21.6	52.3	13.3
8	ZrO ₂	3	19.7	17.4	18.0	48.9	15.7
9	ZrO ₂	5	24.3	23.1	13.5	45.7	17.7
10	La ₂ O ₃	1	6.05	19.5	52.4	18.8	9.29
11	La ₂ O ₃	3	10.1	30.3	42.5	16.9	10.3
12	La ₂ O ₃	5	17.9	55.5	24.4	10.8	9.30
13	MgO	1	16.0	21.6	49.8	20.4	8.24
14	MgO	3	38.2	34.9	38.9	17.1	9.06
15	MgO	5	63.4	52.1	23.7	14.5	9.68
16	CaO	1	18.4	16.2	55.6	18.2	9.97
17	CaO	3	40.7	32.8	41.4	15.1	10.7
18	CaO	5	61.7	50.6	25.6	13.6	10.2

^aReaction conditions: cyclobutanone:DMC = 1:4, time = 5 h, catalyst wt % = 1.5%. ^bThe amount of K₂CO₃, NaOH and CH₃ONa equaled to the amount of basic sites of MgO. ^cDMG = dimethyl glutarate; CMCB = carbomethoxycyclobutanone; ACP = aldol condensation products of cyclobutanone (2-cyclobutylidenecyclobutanone); MP = methyl products (2-methyl-cyclobutanone + dimethyl 2-methylglutarate). ^dSelectivity of dimethyl 2-methylglutarate was 43.7%.

products (methanol and carbon dioxide) were also detected. Table 2 gives the catalytic performance of the different solid catalysts in the synthesis of DMG from cyclobutanone with DMC. In the absence of catalyst, no products were detected. Over solid acids such as zeolite H β and Al₂O₃, the aldol condensation products of cyclobutanone and a little amount of DMG and CMCB were detected, indicating that solid acids are ineffective catalysts for the methoxycarbonylation reaction. However, the reaction was efficiently catalyzed by solid bases. Among those bases, MgO, which possessed the moderate basic strength, exhibited the high performance. ZrO₂ and La₂O₃ gave lower DMG yields, which might be due to their relative weak basic numbers than MgO. As for CaO, it provided slightly lower cyclobutanone conversion and DMG selectivity despite its high basic numbers. This could be attributed to that the acid strength of Ca cation was too weak to stabilize the carbanion species.²⁴ It should be noted that MgO even showed higher DMG selectivity than simple homogenous catalysts (K₂CO₃, NaOH and CH₃ONa) with the same amount of basic sites. As a result, the catalytic performance is strongly dependent on both basic number and basic strength, and basic sites with moderate strength are most effective for the synthesis of DMG from cyclobutanone with DMC.

In order to further examine the effect of moderate basic strength on catalytic performance, a series of MgO catalysts with different Al contents were prepared to provide materials

**Figure 3.** The relationship between the amount of basic sites and DMG yield.**Figure 4.** The relationship between the amount of MgO catalyst and DMG yield.

with different amounts of moderate basic sites (see Figure 2). It was found that the addition of alumina did not change the basic character of MgO, but the basic number of moderate basic sites decreased with the increasing Al contents. For MgO-based catalysts, a good linear correlation between the DMG yield and the amount of moderate basic sites was observed between (see Fig. 3). Moreover, a similar tendency was also observed when the amount of pure MgO catalysts was changed (see Figure 4). Therefore, these results indicated that base sites with moderate strength favored the formation of DMG.

The effect of recycling the MgO catalyst in the reaction of DMC with cyclobutanone is shown in Table 3. It was found that cyclobutanone conversion decreased by 27.7% and DMG selectivity decreased by 22.8% after the catalysts were used five times. Meanwhile, the selectivity of dimethyl 2-methyladipate reached 42.3%, which was comparable with that of K₂CO₃ (see Table 2). These results may suggest that the generation of Mg carbonate salts, due to the formation of carbon dioxide in the methylation reaction, was the reason for deactivation of the catalyst. Fortunately, the used cata-

Table 3. The recycling of MgO in the reaction of cyclobutanone and DMC

Catalyst ^a	Cyclobutanone conversion (%)	Selectivity (%)				
		DMG	CMCB	dimethyl 2-methylglutarate	2-methyl-cyclobutanone	2-cyclobutylidene-cyclobutanone
MgO ^a	63.4	52.1	23.7	7.03	2.67	14.5
MgO (r1) ^b	53.6	47.2	10.8	17.5	2.98	21.5
MgO (r2) ^b	45.5	40.6	8.05	27.4	5.02	18.9
MgO (r3) ^b	40.7	35.1	5.31	34.9	5.99	18.7
MgO (r5) ^b	35.7	29.3	2.78	42.3	6.54	19.1
MgO (r1) ^{*c}	61.9	51.7	20.6	10.9	3.29	13.6
MgO (r2) ^{*c}	62.6	50.4	18.7	13.6	5.51	11.8
MgO (r3) ^{*c}	60.3	49.4	21.0	14.3	6.99	8.31
MgO (r5) ^{*c}	60.9	47.8	17.8	15.9	6.54	12.0

^aReaction conditions: T = 260 °C, cyclobutanone:DMC = 1:4, time = 5 h, catalyst wt % = 1.5%. ^bThe used catalysts were separated by filtration and washed with 20 mL of methanol three times, and then used for the next run. ^cThe used catalysts obtained by calcination at 500 °C for 5 h under nitrogen atmosphere after filtration from the reaction mixture

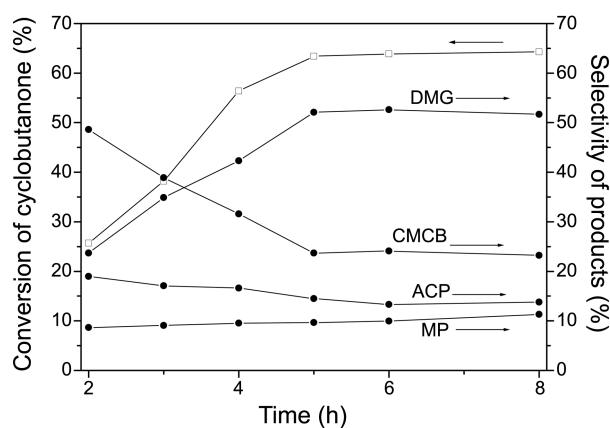


Figure 5. Effect of reaction time on the conversion of cyclobutanone and selectivity of products over MgO. Reaction conditions: T = 260 °C, cyclobutanone:DMC = 1:4, catalyst wt % = 1.5%. DMG = dimethyl glutarate; CMCB = carbomethoxycyclobutanone; ACP = aldol condensation products of cyclobutanone (2-cyclobutylidene-cyclobutanone); MP = methyl products (2-methyl-cyclobutanone + dimethyl 2-methylglutarate).

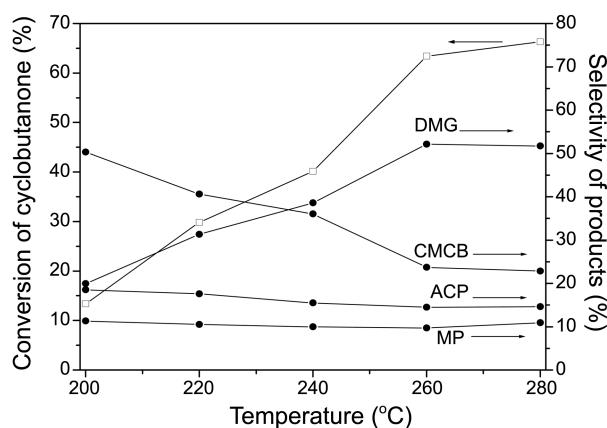


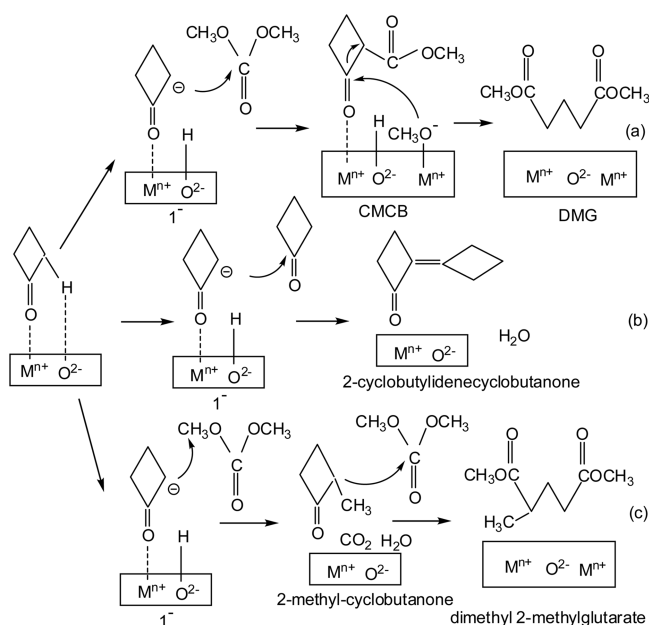
Figure 6. Effect of reaction temperature on the conversion of cyclobutanone and selectivity of products over MgO. Reaction conditions: time = 5 h, cyclobutanone:DMC = 1:4, catalyst wt % = 1.5%. DMG = dimethyl glutarate; CMCB = carbomethoxycyclobutanone; ACP = aldol condensation products of cyclobutanone (2-cyclobutylidene-cyclobutanone); MP = methyl products (2-methyl-cyclobutanone + dimethyl 2-methylglutarate).

lysts could be regenerated by calcination even after having been used several times (see Table 3).

Plausible Reaction Mechanism. Figure 5 shows the influence of reaction time on the reaction of DMC with cyclobutanone over MgO. As can be seen, the conversion of cyclobutanone gradually increased with reaction time, and then reached a stable value after 5 h (see Figure 5). After that time, the conversion of cyclobutanone and yield of products remained essentially unchanged (see Figure 5). Interestingly, the selectivity of DMG increased with prolonged reaction time, whereas the reverse change was observed for the selectivity of CMCB, whilst the selectivity of the other products remained almost unchanged. Similar trends were also observed for the effect of varying reaction temperature (see Fig. 6). These results suggest that the reaction proceeds *via* CMCB as the intermediate. Our group has previously reported that DMC is hardly activated on solid bases.²² Thus, a plausible reaction mechanism for the synthesis of DMG

can be proposed as follows (see Scheme 1(a)): initially, a proton is abstracted from cyclobutanone to form a carbanion of cyclobutanone (1^-), and then 1^- and the proton were absorbed on acidic sites (M^{n+}) and basic sites (O^{2-}) of the solid base surface, respectively. Afterwards, 1^- attacked the carbonyl group of a DMC molecule, which produced CMCB as the primary product. After that, the resulting intermediate reacted with a methoxide anion to yield the corresponding carbanion, which was subjected to ring-opening giving DMG as the final product.

A similar anionic mechanism has also been proposed for the condensation of cyclobutanone (to give 2-cyclobutylidene-cyclobutanone) and the products of methylation of cyclobutanone with DMC (2-methyl-cyclobutanone and dimethyl 2-methylglutarate). As shown in Scheme 1(b), 1^- could attack a second cyclobutanone molecule to produce 2-cyclobutylidene-cyclobutanone and water. Likewise, 1^- can abstract the methyl group of DMC to produce the methyl-



Scheme 1. A plausible mechanism for the reaction of cyclobutanone with DMC.

ation product 2-methyl-cyclobutanone, which formed methanol and carbon dioxide at the same time. Afterwards, the anion of 2-methyl-cyclobutanone can react with another molecule of DMC to give dimethyl 2-methylglutarate as a further product (see Scheme 1(c)).

Conclusions

The synthesis of DMG from cyclobutanone with DMC can be carried out over solid base catalysts. The results revealed that MgO, which possesses moderate basic strength, showed the best performance among the solid bases investigated. The role of the basic catalysts was mainly attributed to activation of the cyclobutanone *via* abstraction of a proton in the α -position by base sites, and a possible reaction pathway, which includes CMCB as an intermediate was proposed. Under the optimal conditions, using MgO as a catalyst, the cyclobutanone conversion and the DMG selectivity reached 63.4% and 52.1%, respectively.

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